

teaches the external administration of the compounds of the present invention in the treatment of lupus erythematosus. The Examiner argues that the compounds are pharmaceuticals, which would motivate one skilled in the art to prepare compositions containing them for treating Lupus erythematosus topically. The Examiner concludes that the claimed method of treatment and topical compositions are obvious over the art. Applicants respectfully disagree and traverse the rejection.

In this rejection the Examiner has missed a crucial point in the Fujisawa teachings - the indication "Lupus erythematosus" on page 67, line 3, is preceded by the term "systemic". The implication of this is twofold. First, it indicates that the inventors had no conception that their compounds could be used topically for the treatment of cutaneous manifestations of Lupus erythematosus. All of the conditions disclosed by Okuhara require systemic treatment; and in all of the examples of the reference, the compounds are administered orally or parentally, that is systemically. There is no example of a condition, which can be treated locally; and as indicated in the Amendment of April 29, 1996 on the instant application, even the fungi used in the antimicrobial test 2, *Aspergillus fumigatus* and *Fusarium oxysporum*, are organisms which are treated systemically. No testing was carried out with organisms, such as dermatophytes or yeast fungus, which would show topical efficacy. As discussed on pages 2 and 3 of the specification, the topical efficacy of the claimed compounds is totally unexpected in light of the results found with the known cyclic immunosuppressant, cyclosporine. There is clearly nothing in Okuhara as a whole which would suggest that, unlike the prior

art immunosuppressant, the claimed compounds would exhibit surprising topical activity; and there is certainly nothing which would motivate one skilled in the art to investigate the topical treatment of the cutaneous manifestations of Lupus erythematosus.

The second implication, which one skilled in the art would draw from Okuhara is that the external administration contemplated by the reference clearly involves those modes of administration, such as the nasal, buccal, rectal, etc. routes, which would produce a systemic effect. Okuhara's pharmaceutical forms listed of on page 76, lines 18 and 19, include only forms which can be administered in these manners such as suppositories. Applicants' lotions, gels, and creams cannot be administered by these routes or used for systemic administration of a drug. No one would reasonably consider treating a condition systemically by topically administering a drug in a lotion, gel, or cream at a cite distant from the point where it exerts its activity. The purpose of topical administration with these forms is to obtain a non-systemic beneficial effect at the site of administration. Okuhara does not disclose a non-systemic use for the claimed compounds, and the cyclosporin art teaches that such compounds are generally not effective when administered in conventional topical forms. It is clear that Applicants method of treatment and pharmaceutical compositions could only be arrived at by disregarding the teachings of the Okuhara patent and the prior art as a whole. There is no way that one skilled in the art using the reference examples alone would be led to Applicants' invention without direction

from the instant application. The Court of Customs and Patent Appeals indicated In re Taborsky (183 USPQ 50), that for obviousness, the prior art must provide one with motivation to make the modifications needed to arrive at the claimed invention. In the present case, the prior art would not only not motivate one to make the topical modifications required to obtain the instant invention, but would lead one away from it. Applicants believe that the presently claimed topical compositions and method of treating the cutaneous manifestations of Lupus erythematosus are clearly patentable over the Okuhara, et al. application; and accordingly, it is respectfully requested that the Examiner reconsider the instant rejection under 35 USC 103 and withdraw it.

Claims 19 to 26 and presumably new claim 28 are again rejected for obviousness-type double patenting over the claims of U.S. Patent No. 5,366,971. As indicated in the Amendment of April 29, 1996 on the instant application, Applicants will submit a Terminal Disclaimer in accordance with the requirements of Rule 78(d) and Rule 321(b), to disclaim the portion of the term of any patent, that issues on the present application with claims embracing the subject matter of present claims 19 to 26 and 29, which extends beyond November 22, 2011, the expiration date of United States Patent 5,366,971. The disclaimer will also state that any patent issuing on this application shall be enforceable only for and during such period that the ownership of this patent is the same as the ownership of USP 5,366,971.

Applicants have added new claims 27 and 28 to cover preferred embodiments of the invention. The basis for the new claims is found in compound A and C on page 14. The new claims are fully supported by the present application, and it is respectfully requested that they be entered. These claims were not presented earlier, because it was only during a review of the application in conjunction with the instant Office Action that the absence of claims covering the unprotected hydroxy compounds was noted. The subject matter of the new claims has essentially been considered by the Examiner, and the claims will not require further examination or raise any new issues of patentability.

Applicants have also amended pages 6 and 13 of the specification and claims 14 and 20 to correct minor errors in spelling, nomenclature, and punctuation.

It is respectfully requested that the period for filing a response to the Office Action of July 23, 1996 on the above identified application Serial No. 08/471,146 originally set to expire October 23, 1996 be extended for two months until December 23, 1996.

Please charge the extension fee of \$390.00 required by 37 CFR 1.17(b) to Deposit Account No. 19-0134 in the name of Sandoz Corporation.

In view of the above amendments and comment, it is believed that the claims now in the application are patentable over the prior art and in condition for allowance. Accordingly, it is respectfully requested that the Examiner withdraw the present rejection of the claims and pass the application to issue, conditioned on the filing of the terminal disclaimer, if claims 19 to 26 and 28 are found to be allowable.

Respectfully submitted,

By Thomas O. McGovern  
Thomas O. McGovern  
Registration No. 25,741  
(201) 503-8480

TOM:lmc

SANDOZ CORPORATION  
59 Route 10  
E. Hanover, N.J. 07936

December 20, 1996

Encl.: Copy of page 6 in duplicate;  
Notice of Appeal (3)